REMARKS

Favorable reconsideration and allowance of the present application are respectfully requested in view of the following remarks.

Currently, claims 82-96 are pending in the present application, including independent claim 82. Independent claim 82, for instance, is directed to a method for simultaneously detecting the presence of at least two metalloproteinases in a chronic wound of a human or an animal. The method comprises collecting a sample of fluid from the chronic wound and exposing the sample to a plurality of target antibodies including a first target antibody that is configured to bind with a first metalloproteinase to form a first target antibody/metalloproteinase complex and a second target antibody that is configured to bind with a second metalloproteinase to form a second target antibody/metalloproteinase complex. The first metalloproteinase is identified by determining the presence or absence of a detectable or measurable manifestation of a first signal element bound to the first target antibody and the second metalloproteinase is identified by determining the presence or absence of a detectable or measurable manifestation of a second signal element bound to the second target antibody.

In the Office Action, the Abstract was objected to. Applicants submit that the presently presented Amendments to the Abstract answer these objections.

In the Office Action, claim 90 was rejected under 35 U.S.C. §112, first paragraph. Specifically, it was stated that the specification does not reasonably provide enablement for identifying two or more metalloproteinases using the same signal element. It was also stated that the specification teaches the structure of no representative species of such methods, and it was stated that the claim introduces New Matter by introducing the limitation "wherein the first signal element and the second signal element are the same."

In response, the Applicants respectfully direct the Examiner's attention to the specification and specifically to Figures 1C, 3 and 4; page 7, lines 3-15; and page 10, line 5 through page 11, line18, which describe representative species of a method such as that found in claim 90. These particular sections of the specification describe various

embodiments of the invention in which a single signal element can be utilized with multiple target antibodies to detect multiple MMP's.

For instance, the embodiments illustrated in Figures 1C, 3 and 4 include multiple reaction sites. The reaction sites are labeled with the reference character 2 (the general reference to a reaction site) and reference characters 20, 21, 22, 23, 24, and 25 (which differentiate between specific reaction sites on a single sensor). As described in the paragraph beginning at page 10, line 28 (as amended in the response dated March 28, 2005) and with reference to Figure 4 (as amended in the response dated March 28, 2005), a sample can be added to the sample chamber (40) of a sensor (10), which contains polystyrene beads coated with target antibodies and a dye. Each reaction site has different capture antibodies bondable to only one proteinase enzyme. The conjugate formed in each reaction site results in an increasing concentration of beads containing the dye molecule. Any reaction sites with color indicate the presence of an enzyme, and sites without color indicate that enzyme was not present in the sample. Thus, a single signal element (e.g., a single dye) can be utilized to detect the different MMP's in a single, simultaneous detection regime, as the specific capture reagents can be isolated in different reaction sites.

Applicants respectfully submit that claim 90 fully complies with 35 U.S.C. §112 and request withdrawal of the rejection.

In the Office Action, claims 82-96 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sorsa et al. (U.S. Patent No. 5,736,341) in view of Rowe et al. (*Anal. Chem.*, **71**, (1999) 3846-3852), and further in view of Sodek et al. (*MATRIX Supplement No. 1*, (1992) 352-362).

Applicants respectfully submit that the above-listed references fail to disclose or suggest certain limitations of the pending claims. For instance, the cited references, taken alone or in any combination, fail to disclose or suggest a method as is found in the pending claims for simultaneously detecting a plurality of metalloproteinases in a sample.

As pointed out in the Office Action, Sorsa et al., does not teach a method for detecting a plurality of metalloproteases. In fact, Sorsa et al. teaches the detection of only one specific MMP, MMP-8, in either the active or pro-form. According to the patent, MMP-8 is "the primary cause of gingival tissue destruction in periodontal disease" (col. 9, ll. 47-53). Other MMPs were considered in the patent, but when GCF was examined by Sorsa et al. for detection of a second MMP via Western blot analysis, "MMP-1 was not detected. MMP-1 was not detected by specific ELISA recording either." While GCF from periodontitis patients was found to contain increased amounts of MMP-8, hardly any immunoreactive fibroblast-type MMP-1 was found. (Col. 17, ll. 45-60.) Hence, Sorsa et al. teaches that only MMP-8 need be detected in diagnosing periodontitis, and provides no incentive for the detection of multiple MMPs.

In the Office Action, Sorsa et al. was combined with Rowe et al. and further with Sodek et al. in an attempt to arrive at the limitations of the pending claims. Rowe et al. discloses an array biosensor for simultaneously detecting the presence of diverse analytes of different classes, and specifically for detecting and separating bacterial (*Bacillus globigii*), viral (MS2 bacteriophage), and protein (staphylococcal enterotoxin B) analytes in a mixture. Bacteria and virus may incorporate proteins, but they are not proteins. Rowe et al. does not describe a method for detecting a plurality of proteins in a mixed sample.

Sodek et al., describes studies of the role certain MMPs play in connective tissue destruction that occurs as a consequence of inflammatory disease, with particular emphasis on the role of collegenase and gelatinase in periodontal disease. Sodek et al., does not, however, teach a fast, convenient method for the simultaneous identification of a plurality of metalloproteases.

Accordingly, Applicants maintain that even if combined as suggested, the combined references still fail to suggest or disclose a method for detecting the presence of at least two metalloproteinases in a sample from a chronic wound, as is found in the pending claims.

Moreover, Applicants further submit that no proper incentive exists to combine the references as suggested. For instance, Applicants submit that no proper incentive exists for combining Rowe et al., with Sorsa et al. and Sodek et al. as suggested in the Office Action.

As mentioned above, Rowe et al. discloses a method for detecting diverse analytes in a mixed sample. Specifically, Rowe et al. discloses a method for detecting a bacterial analyte, a viral analyte and a protein in a mixed sample. The bacterial analyte, *Bacillus globigii*, is a nonpathogenic, Gram-positive, sporulating soil bacterium. The viral analyte is MS2 bacteriophage, a small, icosahedral RNA bacteriophage, and the protein is a toxin, staphylococcal enterotoxin B, which is it is excreted by the *Staphylococcus aureus* bacterium and is a common cause of food poisoning. Not only are these three analytes from completely different classes, but none of them are catabolic enzymes secreted by human and animal cells, as are the matrix metalloproteinases discussed in both Sorsa et al. and Sodek et al. Applicants respectfully submit that no proper incentive exists for one of ordinary skill in the art to combine the teachings of Rowe et al., directed to detecting vastly different analytes, none of which are produced by human or animal cells, with the teaching of either Sorsa et al. or Sodek et al., which are at least tangentially related in that they both discuss periodontal disease and cellular secretions that occur during that particular disease process. At least for the reason that the biotechnology field in general describes a high level of unpredictability, Applicants maintain that the proper incentive for the suggested combination does not exist. Accordingly, Applicants respectfully request withdrawal of the rejection.

At least for the reasons set forth herein, Applicants respectfully maintain that the present application is in complete condition for allowance and favorable action, is therefore requested. Examiner Swope is invited and encouraged to telephone the undersigned, however, should any issues remain after consideration of this Response.

Please charge any additional fees required by this Response to Deposit Account No. 04-1403.

Respectfully requested,

DORITY & MANNING, P.A.

Jason W. Johnston
Registration No: 45,675
P.O. Box 1449
Greenville, SC 29602-1449
Phone: (864) 271-1592
Facsimile: (864) 233-7342

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